Cardiopulmonary Exercise Testing: Basics of Methodology and Measurements

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Abstract

Cardiopulmonary exercise testing adds measurement of ventilation and volume of oxygen uptake and exhaled carbon dioxide to routine physiological and performance parameters obtainable from conventional exercise testing, furnishing an all-around vision of the systems involved in both oxygen transport from air to mitochondria and its use during exercise. Peculiarities of cardiopulmonary exercise testing methodology are the use of ramp protocols and calibration procedures for flow meters and gas analyzers. Among the several parameters provided by this technique, peak oxygen uptake, first and second ventilatory thresholds, respiratory exchange ratio, oxygen pulse, slope of ventilation divided by exhaled carbon dioxide relationship, exercise oscillatory ventilation, circulatory power, and partial pressure of end-tidal carbon dioxide are among the most relevant in the clinical setting. The choice of parameters to be considered will depend on the indication to cardiopulmonary exercise testing in the individual subject or patient, namely, exercise tolerance assessment, prognostic stratification, training prescription, treatment efficacy evaluation, diagnosis of causes of unexplained exercise tolerance reduction, or exercise (patho)physiology evaluation for research purposes. Overall, cardiopulmonary exercise testing is a methodology now widely available and supported by sound scientific evidence. Despite this, its potential still remains largely underused. Strong efforts and future investigations are needed to address these issues and further promote the use of cardiopulmonary exercise testing in the clinical and research setting.

Keywords: exercise; gas exchanges; ventilation; oxygen uptake; exhaled carbon dioxide

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Cardiopulmonary exercise testing joins ventilation and volume of oxygen uptake ($\dot{V}O_2$) and exhaled carbon dioxide ($\dot{V}CO_2$) to routine physiological and performance parameters measured during incremental exercise testing, such as heart rate, blood pressure, work rate, and exercise duration. Therefore, this methodology markedly increases the amount of information obtainable from conventional exercise testing, furnishing an all-around vision of the systems involved in both O_2 transport from air to mitochondria and its use during exercise. Gas exchange measurements during exercise have been demonstrated to enhance the decision-making process in several clinical settings, and cardiopulmonary exercise testing indications entail functional capacity assessment, prognostic stratification, training prescription, treatment efficacy evaluation, diagnosis of causes of unexplained reduced exercise tolerance, and exercise pathophysiology evaluation in an extremely wide spectrum of clinical pictures (1–7). The basic parameters peculiar to cardiopulmonary exercise testing (i.e., ventilation and $\dot{V}O_2$ and $\dot{V}CO_2$) are now routinely obtainable in spreadsheet format by all commercially available systems, providing an easy-to-use platform for straightforward data processing and interpretation.

Methodology

Ventilation parameters and respiratory gases can be collected using a face mask or a mouthpiece, with the choice between the two more linked to a given laboratory's habits than to specific advantages. A face mask allows patient swallowing, which a mouthpiece does not. On the other hand, some patients may feel uncomfortable using a face mask because of lack of air sense. In any case, every laboratory should give patients a choice between a face mask and a mouthpiece, according to their preferences. Cardiopulmonary exercise tests can be performed using incremental or

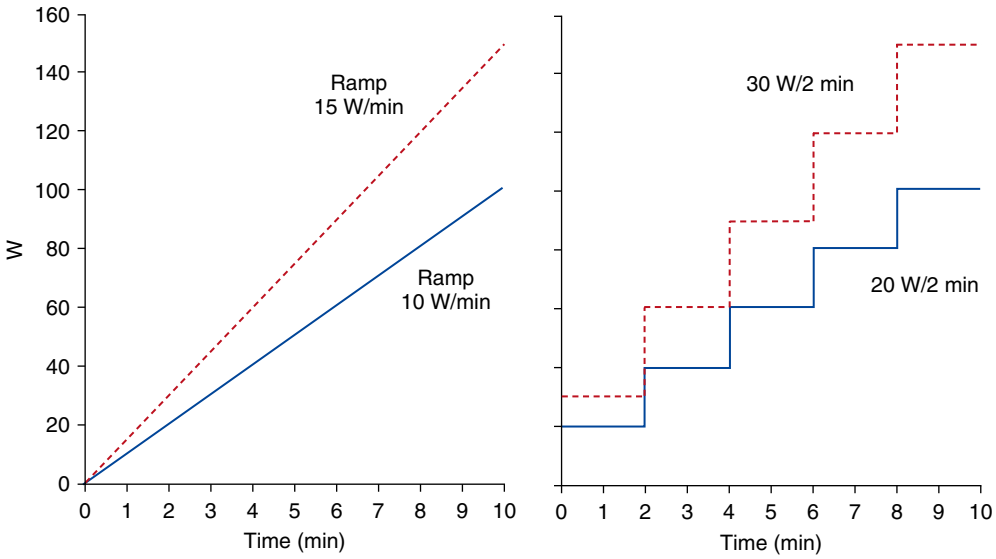

Figure 1. Ramp incremental (*left panel*) and 2-minute incremental (*right panel*) protocols for cycle ergometry. *Red dashed lines* represent protocols reaching an equal work rate of 150 W after 10 minutes of exercise; *blue solid lines* represent protocols reaching an equal work rate of 100 W after 10 minutes of exercise. The work rate increment is added at the start of each 2-minute stage for the conventional incremental test, whereas the increment is equal to 1 W every 6 seconds and 1.5 W every 6 seconds for the 10 W/min and 15 W/min ramp protocols, respectively, beginning from Time 0 of the exercise period.

constant work rate protocols, according to work rate progressive increase or constancy during the test, respectively. Incremental tests are aimed at maximally stressing the O_2 transport and use system and are routinely used in the clinical setting, whereas constant work rate tests are usually performed at submaximal effort intensities and mainly used for research purposes. Among incremental protocols, the ramp-like ones are preferred to conventional incremental tests whenever possible (Figure 1). Ramp protocols are characterized by a gradual increase of work rate, evenly distributed within each minute of the exercise phase (8). For example, on a cycle ergometer, a 10-W/min ramp protocol (which is frequently used in the clinical setting) increases the work rate by 1 W every 6 seconds.

Several ramp grades are commonly used for patients, with 5 W/min, 7 W/min, 10 W/min, and 15 W/min the most popular. The choice of ramp protocol steepness should be tailored to the subject's exercise tolerance, aiming at a test duration ranging between 8 and 12 minutes. The advantage of ramp protocols is twofold: first, the work rate increase is devoid of brisk step increases typical of step protocols (e.g., 25 W every 3 minutes); second, the trend of parameters changes over time is not affected by protocol steps, making physiological responses linear and more readable for the operators. Cardiopulmonary exercise tests can be performed on different kinds of ergometers (i.e., cycle ergometer or treadmill), the pros and cons of which are summarized in Table 1. Of note, ramp incremental protocols are much easier to implement when a cycle ergometer is used.

Cardiopulmonary exercise testing systems contain flow meters and gas analyzers that allow for breath-by-breath measurement of ventilation and the $\dot{V}O_2$ and $\dot{V}CO_2$. As flow meters and gas analyzers are prone to drift, all systems should be calibrated immediately before each test, and the test should not be performed if proper calibration is not confirmed. Response times of the analyzers and transport delay between sampling point and analyzers must be systematically checked as well. In addition, because ambient conditions affect the concentration of oxygen in the inspired air, temperature, barometric pressure, and humidity should also be taken into account. Calibration procedures are automatically performed by all commercial cardiopulmonary exercise testing software.

Table 1. Use of treadmill versus cycle ergometer for cardiopulmonary exercise testing

	Treadmill	Cycle Ergometer
Higher peak oxygen uptake	X	
Easier implementation of ramp protocols		X
Possibility to quantify external work		X
Higher ECG quality		X
Possibility to obtain blood specimens during exercise		X
Higher safety		X
Possible use in supine position		X
Smaller size		X
Less noisy		X
Lower cost		X
Ease of movement		X
Greater experience in Europe		X
Greater experience in the United States	X	

Peak $\dot{V}O_2$

$\dot{V}O_2$ is measured in liters or milliliters of oxygen per minute or in milliliters per kilogram of body weight per minute and is defined by the Fick principle: $\dot{V}O_2$ equals cardiac output (CO) × $C(a–v)O_2$, where $C(a–v)O_2$ is the arteriovenous oxygen content difference (5). Peak oxygen uptake ($\dot{V}O_{2Peak}$) is a parameter describing the maximal amount of energy obtainable by aerobic metabolism per unit of time (aerobic power) at peak incremental exercise and is defined as the highest volume of $\dot{V}O_2$, averaged over a 20- to 30-second period, achieved at presumed maximal effort during an incremental cardiopulmonary exercise test. $\dot{V}O_{2Peak}$ is known to describe patient exercise tolerance far more reliably than performance descriptors obtainable by conventional exercise testing, such as exercise duration or peak work rate (1).

$\dot{V}O_{2Peak}$ declines on average by 10% per decade after the age of 30, due to decreasing maximal heart rate, stroke volume, blood flow to skeletal muscle, and skeletal muscle aerobic potential with decreasing age (9) (Table 2). In addition, $\dot{V}O_{2Peak}$ is 10 to 20% greater in men than in women of comparable age (10), because of higher hemoglobin concentration and greater muscle mass and stroke volume in men (Table 2).

All pathophysiological states impairing oxygen transport from air to mitochondria and its use during exercise will determine some degree of reduction of $\dot{V}O_{2Peak}$ with respect to predicted values according to age and sex. This is commonly observed not only in several different organ and system diseases, such as chronic heart failure (11), chronic obstructive pulmonary disease (12), amyotrophic lateral sclerosis (13), mitochondrial myopathies (14), and so forth but also in bed-rest deconditioning (15).

Of note, $C(a–v)O_2$ increases linearly with work rate progression during incremental exercise, and its value is relatively fixed at peak effort in both normal subjects and patients. Accordingly, peak CO is indirectly determinable according to the Fick principle (*see above*) using estimated peak $C(a–v)O_2$ and measured $\dot{V}O_{2Peak}$ (16).

Ventilatory Thresholds

During incremental exercise, an energy requirement is reached above which anaerobic metabolism is activated, with blood lactate concentration increasing above baseline level at a progressively steeper rate (2, 5, 17, 18). Almost all hydrogen ions generated in the cell from lactic acid dissociation are buffered by

Table 2. Normal values

Parameters	Normal Values			Formulae
$\dot{V}O_{2Peak}$, ml/min	Age (*yr*)	M*	W*	Sedentary men:†
	20–29	3,250–2,970	2,000–1,840	[50.72 − (0.372 × age)] × weight
	30–39	2,950–2,690	1,820–1,660	
	40–49	2,670–2,400	1,640–1,490	Sedentary women:†
	50–59	2,380–2,130	1,470–1,320	[22.78 − (0.17 × age)] × (weight + 43)
	60–69	2,110–1,840	1,300–1,140	
	70–80	1,820–1,570	1,120–940	
1stVT oxygen uptake	>40% predicted $\dot{V}O_{2Peak}$ 40–60% measured $\dot{V}O_{2Peak}$			—
Peak oxygen pulse, ml/beat		M*	W*	Predicted $\dot{V}O_{2Peak}$/predicted peak heart rate
	20–29	16.2–15.6	10.0–9.6	
	30–39	15.5–14.9	9.6–9.2	
	40–49	14.8–14.1	9.1–8.7	
	50–59	14.0–13.2	8.6–8.2	
	60–69	13.1–12.2	8.1–7.5	
	70–80	12.1–11.1	7.4–6.7	
$\dot{V}E/\dot{V}CO_2$ slope		M	W	Sedentary men:‡ 0.12 × age + 21
	20–39	23.4–25.7	26.8–28.3	Sedentary women:‡ 0.08 × age + 25.2
	40–59	25.8–28.1	28.4–29.9	
	60–80	28.2–30.6	30.0–31.6	
Peak circulatory power, ml/kg/min × mm Hg		M§	F§	—
	20–39	8,600–7,000	6,660–5,600	
	40–59	7,050–5,680	5,480–4,400	
	60–80	5,630–4,200	4,320–3,140	
1stVT partial pressure of end-tidal carbon dioxide, mm Hg	3- to 8-mm Hg increase with respect to resting value			—

Definition of abbreviations: 1stVT = first ventilatory threshold; M = men; $\dot{V}CO_2$ = volume of exhaled carbon dioxide; $\dot{V}E$ = ventilation; $\dot{V}O_{2Peak}$ = peak oxygen uptake; W = women.
*Values are calculated for men of 75 kg and women of 60 kg weight.
†Formulae for normal-weight subjects according to Reference 20, which also reports formulae for under- and overweight subjects.
‡Formulae for normal subjects according to Reference 20.
§Values are calculated for men of 75 kg and women of 60 kg weight, using $\dot{V}O_{2Peak}$ values reported above and a peak systolic blood pressure value of 200 mm Hg.

bicarbonate, yielding an excess carbon dioxide amount that makes the $\dot{V}_{CO_2}$ versus $\dot{V}_{O_2}$ relationship become steeper. By measuring at the mouth gas exchange modifications induced by these metabolic changes, the so-called first ventilatory threshold can be identified by analyzing the slope of $\dot{V}_{CO_2}/\dot{V}_{O_2}$ relationship (plotted on equal scales) during ramp incremental exercise (19). Accordingly, the first ventilatory threshold is the point of transition of the slope from less than 1 to greater than 1 (Figure 2, *upper panel*), occurring in the vast majority of subjects and patients between 40 and 60% of $\dot{V}_{O_{2Peak}}$ (20).

With increasing exercise intensity above the first ventilatory threshold, a point in time is reached when intracellular bicarbonates are no longer able to adequately counteract exercise-induced metabolic acidosis. Hyperventilation thus develops through a ventilation increase in excess of $\dot{V}_{CO_2}$, which is termed the second ventilatory threshold or "respiratory compensation point" (Figure 2, *lower panel*) (18) and is usually attained at around 70 to 80% of $\dot{V}_{O_{2Peak}}$.

The first and second ventilatory threshold are important parameters for aerobic training intensity prescription over a wide spectrum of exercise capacities, ranging from top-level athletes to patients with severely reduced exercise performance (21). As a multitude of different (and somewhat confusing) terms are found in the literature describing the two thresholds, the term "ventilatory" thresholds is preferred (22). This is because those two transitions are detected using incremental exercise-induced changes in ventilation-related parameters and not in direct descriptors of metabolic homeostasis alteration (e.g., lactic acid).

Finally, ventilatory thresholds are not always clearly identifiable in patients with severely reduced exercise tolerance, and inability to identify the first ventilatory threshold plays an important negative prognostic role in patients with advanced chronic heart failure (23).

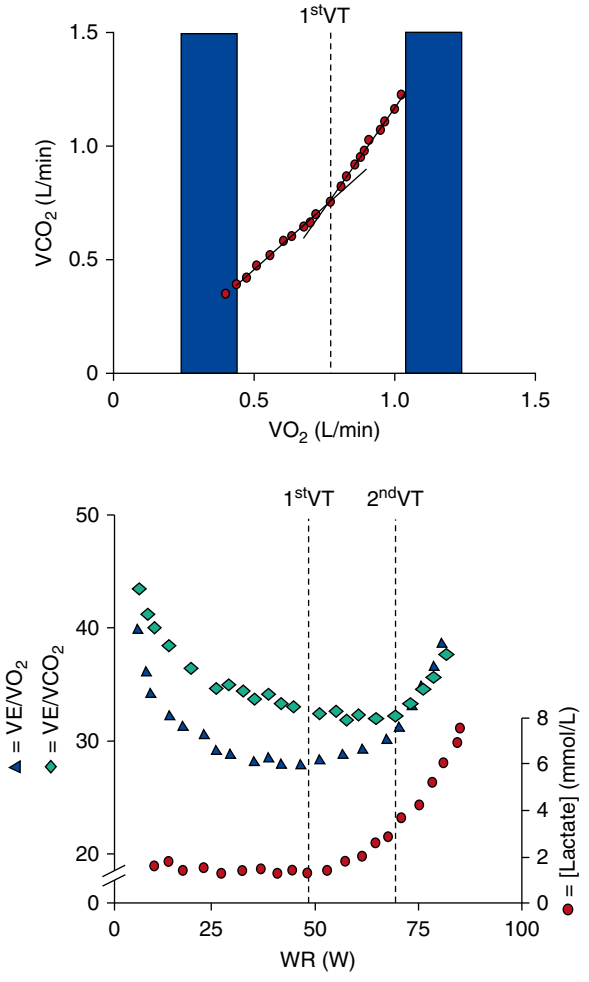

Figure 2. (*Upper panel*) Volume of exhaled carbon dioxide ($\dot{V}_{CO_2}$) as a function of volume of oxygen uptake ($\dot{V}_{O_2}$) during incremental exercise. The point in time when the $\dot{V}_{CO_2}/\dot{V}_{O_2}$ slope increases its steepness due to excess $\dot{V}_{CO_2}$ from lactic acid buffering is the first ventilatory threshold. The initial and final phases of exercise (*blue rectangles*) are usually excluded from the analysis due to possible hyperventilation during these periods. (*Lower panel*) Ventilatory equivalents for oxygen and carbon dioxide as a function of work rate (WR) during ramp incremental exercise. The nadir of the ventilatory equivalent for oxygen ($\dot{V}_E/\dot{V}_{O_2}$) identifies the first ventilatory threshold (i.e., the point in time when ventilatory drive starts increasing relative to $\dot{V}_{O_2}$ due to excess $\dot{V}_{CO_2}$ from anaerobic metabolism activation). The nadir of ventilatory equivalent for carbon dioxide ($\dot{V}_E/\dot{V}_{CO_2}$) identifies the second ventilatory threshold, namely, the point in time when ventilatory drive starts increasing relative to $\dot{V}_{CO_2}$ (i.e., when hyperventilation occurs). $\dot{V}_E$ = ventilation; 1stVT = first ventilatory threshold; 2ndVT = second ventilatory threshold.

Respiratory Exchange Ratio

The respiratory exchange ratio is the ratio between $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$. As discussed above, with increasing exercise intensity, lactic acid buffering generates an excess $\dot{V}_{CO_2}$, which increases the respiratory exchange ratio numerator at a faster rate than the denominator. Therefore, a respiratory exchange ratio higher than 1.00 implies significant anaerobic metabolism activation above the first ventilatory threshold and is further increased by hyperventilation occurring past the second ventilatory threshold. This physiological response to exercise is consistent across healthy subject and patient populations, which makes peak respiratory exchange ratio an objective descriptor of maximal effort attainment and subject motivation (Table 3) (i.e., of a crucial issue to guarantee reliable and clinically meaningful $\dot{V}_{O_{2Peak}}$ values) (24).

Of note, even though a peak respiratory exchange ratio of higher than 1.10 is generally considered to describe a significant exercise-induced whole-body stress, it must not be considered an indication for test interruption. On the other hand, achievement of a peak respiratory exchange

Table 3. Criteria of maximal effort attainment

Failure of oxygen uptake and/or heart rate to increase with further increase in work rate
Peak respiratory exchange ratio ⩾ 1.10–1.15
Post-exercise blood lactate concentration ⩾ 8 mmol/dl
Rating of perceived exertion ⩾ 8 (on the 10-point Borg scale)

ratio lower than 1.00 in the absence of ECG or hemodynamic abnormalities generally reflects submaximal cardiovascular effort. It must be borne in mind, however, that patients with severely impaired exercise tolerance can attain skeletal muscle strength exhaustion even earlier than central hemodynamic and ventilatory factors become limiting, interrupting exercise at peak respiratory exchange ratio values even lower than 1.00. Another possibility for lack of an adequate respiratory exchange ratio increase during incremental exercise is severe chronic obstructive lung disease, wherein lung hyperinflation can hinder hyperventilation past the first ventilatory threshold (5).

Oxygen Pulse

Oxygen pulse is the $\dot{V}O_2$/heart rate ratio and reflects the amount of oxygen consumed per heartbeat (i.e., stroke volume multiplied by $C(a–v)O_2$). Assuming normal values of arterial oxygen content and $C(a–v)O_2$ at peak effort, peak stroke volume in milliliters can then be estimated as (oxygen pulse/15) × 100, where oxygen pulse is in milliliters per beat (5). However, this estimation must be used with caution. The subjects must be normal and motivated and the peripheral oxygen extraction must be ideal to assume a linear relationship between $\dot{V}O_2$ and CO during exercise.

During incremental exercise, the relative contribution of stroke volume to CO is dominant during the initial and intermediate phases of exercise. Thus, oxygen pulse expressed as a function of work rate has a typical hyperbolic profile, with a rapid increase during the initial stages of exercise and a slow approach to an asymptotic value at the end of exercise. A flattening or downward displacement of oxygen pulse kinetics during incremental exercise likely reflects peripheral vascular perfusion or extraction or central cardiogenic performance limitations. Among the latter, the development of exercise-induced myocardial ischemia can be present when a flattening or even decrease of both the oxygen pulse versus work rate (Figure 3) and $\dot{V}O_2$ versus work rate relationships occur at the same time (25). However, it is important to understand that these abnormal responses are nonspecific and can also be seen in other conditions that might impair CO on response during exercise.

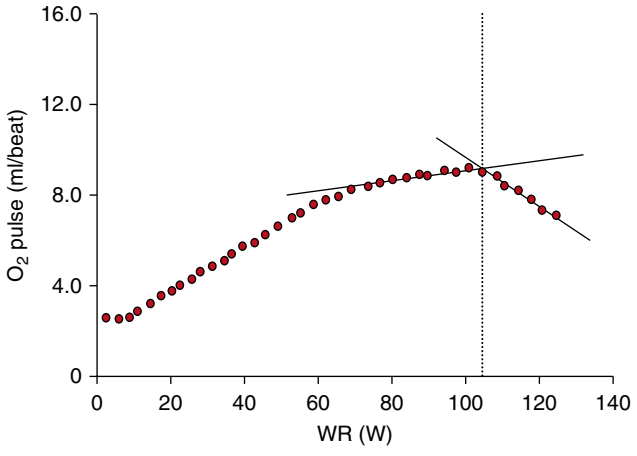

Figure 3. Oxygen pulse as a function of work rate (WR) during ramp incremental exercise in a patient with coronary artery disease. The transition (*dotted line*) from a physiological increase to a decrease in oxygen pulse is considered a possible marker of exercise-induced myocardial ischemia onset. *See* text for further details.

Ventilation and Slope of the Ventilation/$\dot{V}CO_2$ Relationship

From a physiological standpoint, ventilation is equal to $863 \times \dot{V}CO_2/[Pa_{CO_2} \times (1 - V_D/V_T)]$, where $\dot{V}CO_2$ is the volume of exhaled carbon dioxide, Pa_{CO_2} is the partial pressure of arterial carbon dioxide, and V_D and V_T are pulmonary dead space and tidal volume, respectively (18, 26, 27). When plotting ventilation as a function of $\dot{V}CO_2$ during incremental exercise, the slope of such a relationship ($\dot{V}E/\dot{V}CO_2$ slope) describes the patient's ventilatory efficiency (i.e., the amount of air that must be ventilated to exhale 1 L of carbon dioxide) (Figure 4). The physiological meaning of $\dot{V}E/\dot{V}CO_2$ slope is described by rearranging the above equation as follows: $\dot{V}E/\dot{V}CO_2 = 863/[Pa_{CO_2} \times (1 - V_D/V_T)]$. Accordingly, $\dot{V}E/\dot{V}CO_2$ slope will increase when Pa_{CO_2} is reduced by hyperventilation and when V_D/V_T (i.e., wasted ventilation) is high. Another proposed cause of increased $\dot{V}E/\dot{V}CO_2$ slope is effort-induced muscle ergoreflex overactivation (28).

Normal values of $\dot{V}E/\dot{V}CO_2$ slope show a progressive increase with increasing age (20) (Table 2). A higher than normal $\dot{V}E/\dot{V}CO_2$ slope may be of undeterminable origin (i.e., primary hyperventilation) or due to respiratory or cardiac diseases that induce a mismatch of ventilation to perfusion. An increased $\dot{V}E/\dot{V}CO_2$ slope is classically observed in patients with chronic heart failure and in those with pulmonary hypertension of different etiologies, with values progressively higher with increasing disease severity (29–35). Conversely, a downward displacement of the $\dot{V}E/\dot{V}CO_2$ slope occurs when the Pa_{CO_2} set point is raised (i.e., in primary alveolar hypoventilation).

Exercise Oscillatory Ventilation

Oscillatory ventilation during exercise is a slow, prominent, consistent (rather than random) fluctuation of ventilation (Figure 5) that may occur in different patterns (i.e., be present during the entire duration of the exercise phase or only during early or peak exercise) (36, 37). Several pathophysiological determinants of this phenomenon have been proposed, which may be grouped into ventilatory (i.e., instability in the feedback ventilatory

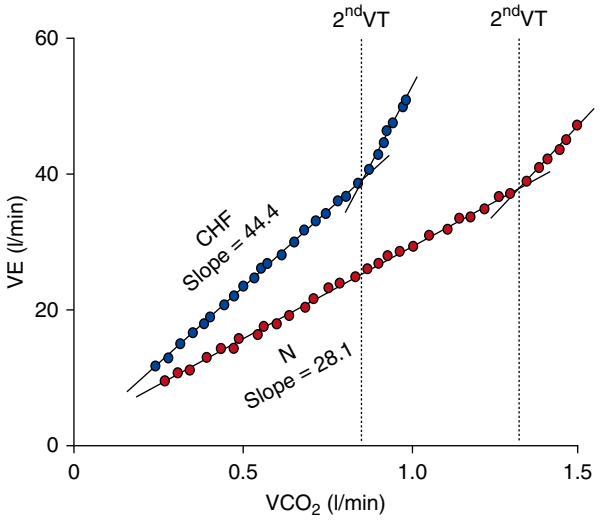

Figure 4. Ventilation ($\dot{V}_E$) as a function of volume of exhaled carbon dioxide ($\dot{V}_{CO_2}$) during ramp incremental exercise in a normal subject and a patient with chronic heart failure. A reduced ventilatory efficiency is present in chronic heart failure, as witnessed by a steeper $\dot{V}_E/\dot{V}_{CO_2}$ slope when compared with that of a normal subject. 2ndVT = second ventilatory threshold; CHF = patient with chronic heart failure; N = normal subject.

control system) and hemodynamic (i.e., pulmonary blood flow fluctuations) (38). The criteria used to identify oscillatory ventilation during exercise suffer from lack of standardization (39), with the most often adopted being those recommended by the American Heart Association (i.e., persistence of an oscillatory ventilation pattern for at least 60% of exercise duration at an amplitude higher than 15% of the average value of ventilation at rest).

Among patients with cardiac disease, exercise oscillatory ventilation is specifically detected in those with chronic heart failure and associated with cyclic changes in arterial oxygen and carbon dioxide tensions. Of note, in this population, exercise oscillatory ventilation is often associated with nocturnal periodic breathing (40, 41).

Circulatory Power

Cardiac power, the product of CO and mean arterial pressure, is a powerful index of cardiac systolic function (42). Circulatory power is a cardiac power surrogate obtainable from cardiopulmonary exercise testing, calculated as $\dot{V}_{O_2}$ (in milliliters per kilogram per minute) multiplied by systolic blood pressure (43). Accordingly, circulatory power represents the triple product of CO × $C(a–v)O_2$ × systolic blood pressure. Of note, unlike invasive assessment of peak cardiac power, peak circulatory power can be easily assessed multiplying $\dot{V}_{O_{2Peak}}$ by peak systolic blood pressure. Normal values of peak circulatory power between 3,000 and 8,000 mm Hg × mL/kg/min are usually found according to age (Table 2), the highest values being found in young athletes and in patients with hypertension with preserved systolic function.

Circulatory power is an interesting parameter summarizing heart rate, stroke volume, blood pressure, and $C(a–v)O_2$ responses to exercise, all of which can be

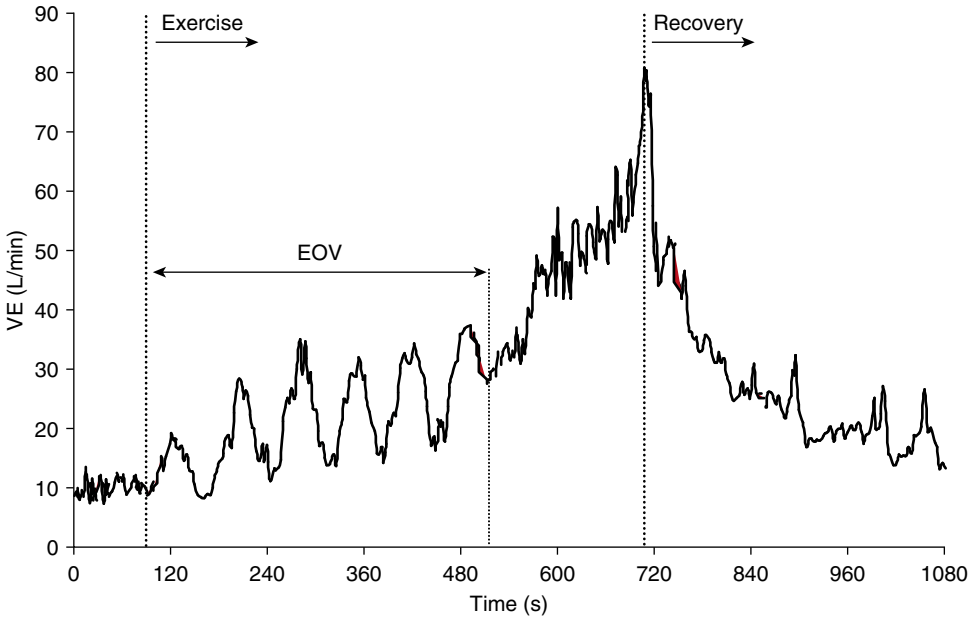

Figure 5. Ventilation ($\dot{V}_E$) as a function of time during ramp incremental exercise in a patient with chronic heart failure. An oscillatory ventilatory pattern is present during exercise, defined as cyclic fluctuations in $\dot{V}_E$ lasting at least 60% of the exercise period, with an amplitude of fluctuations during exercise higher than 15% of the average value of $\dot{V}_E$ at rest. EOV = exercise oscillatory ventilation.

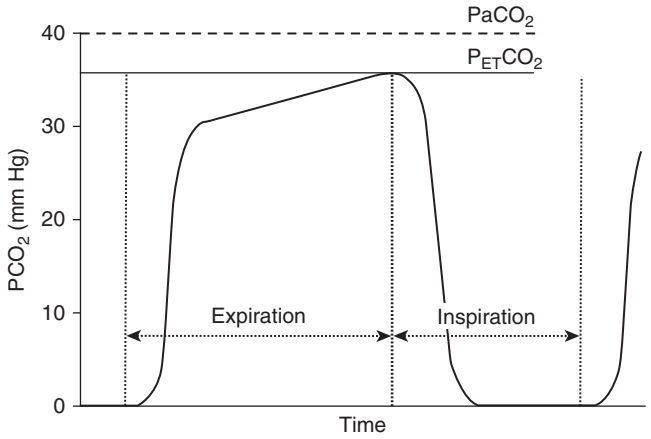

Figure 6. Partial pressure of end-tidal carbon dioxide ($P_{ET}CO_2$) in breathed air during a respiratory cycle as a function of time. $P_{ET}CO_2$ is the carbon dioxide partial pressure at the end of expiration, mirroring (but not being equal to) the partial pressure of alveolar and arterial carbon dioxide. The difference between arterial carbon dioxide partial pressure (Pa_{CO_2}) and $P_{ET}CO_2$ is mainly due to mismatch of ventilation to perfusion.

altered in several pathophysiological conditions, in particular, chronic heart failure. Even if not routinely assessed in the clinical setting, peak circulatory power is a nice example of the possibility provided by cardiopulmonary exercise testing to noninvasively explore left ventricular systolic function during incremental exercise.

Partial Pressure of End-Tidal Carbon Dioxide

The partial pressure of end-tidal carbon dioxide in exhaled air ($P_{ET}CO_2$) is commonly derived in mm Hg units by cardiopulmonary exercise testing instrumentation (Figure 6). Normal values at rest range between 36 and 42 mm Hg, increase from rest to first ventilatory threshold and then decrease as maximal effort is approached (5) (Table 2). Several investigations have demonstrated a significant direct relationship between resting $P_{ET}CO_2$ and CO (44). The $P_{ET}CO_2$ measured at first ventilatory threshold during incremental exercise has also been correlated with CO in patients with chronic heart failure (45) and found to mirror disease severity in this population. However, caution is required in interpreting $P_{ET}CO_2$ values in individual patients, as they may be affected by acute hyperventilation, increased dead space due to emphysema or other lung diseases, or rapid and shallow breathing patterns, all of which will reduce the $P_{ET}CO_2$ independently of cardiac function.

In patients with pulmonary hypertension, $P_{ET}CO_2$ at rest and first ventilatory threshold is related to pulmonary pressures and can thus provide a noninvasive picture of disease severity (32). Changes in $P_{ET}CO_2$ may also be of help in the detection of exercise-induced right-to-left shunting, as testified by (*1*) an abrupt and sustained increase in partial pressure of end-tidal oxygen with a simultaneous sustained decrease in partial pressure of end-tidal carbon dioxide, (*2*) an abrupt and sustained increase in the respiratory exchange ratio, and (*3*) an associated decline in pulse oximetry saturation (46).

Conclusions

Cardiopulmonary exercise testing is a methodology now widely available and supported by sound scientific evidence in several clinical fields. However, the full potential of this technique in the clinical and research setting still remains largely underused. This may be due to several reasons, among which lack of measurements standardization, nonuniform parameter availability in cardiopulmonary exercise testing systems of different manufacturers, inability to easily interpret the obtained information in a way that is specific to test indication, limited availability of data in important subpopulations (such as women), and inertia of professionals in the face of a demanding methodology. Strong efforts and future investigations are needed to address these issues and further promote the use of cardiopulmonary exercise testing in the clinical and research setting. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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